

## **AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

### **Listing of claims:**

- 1-18. (canceled)
19. (currently amended) An immune adjuvant composition comprising
- (a) a saponin possessing immune adjuvant activity, wherein the saponin is derived from *Quillaja saponaria*; and
- (b) an immunostimulatory oligonucleotide comprising at least one unmethylated CpG dinucleotide,
- wherein the immunostimulatory oligonucleotide is not a part of a DNA vaccine vector, and
- wherein the saponin and immunostimulatory oligonucleotide have a synergistic adjuvant effect.
20. (canceled)
21. (previously presented) The immune adjuvant composition as claimed in claim 19, wherein the saponin comprises a substantially pure saponin.
22. (currently amended) The immune adjuvant composition as claimed in claim 21, wherein the substantially pure saponin ~~comprises~~ is QS-7, QS-17, QS-18, or QS-21.
23. (currently amended) The immune adjuvant composition as claimed in claim 22, wherein the substantially pure saponin ~~comprises~~ is QS-21.
24. (currently amended) The immune adjuvant composition as claimed in claim 19 or 23, wherein the immunostimulatory oligonucleotide comprises more than one unmethylated CpG dinucleotide.
25. (currently amended) The immune adjuvant composition as claimed in claim 19 or 23, wherein the immunostimulatory oligonucleotide comprises at least one chemical group selected from the group consisting of phosphorothioate, alkylphosphonate, phosphorodithioate, alkylphosphorothioate, phosphoramidate, 2-O-methyl, carbamate, acetamidate, carboxymethyl ester, carbonate, and phosphate triester.

26. (currently amended) The immune adjuvant composition as claimed in claim 19 or 23, wherein the immunostimulatory oligonucleotide comprises at least one phosphorothioate modified nucleotide.

27. (previously presented) The immune adjuvant composition as claimed in claim 19, wherein the immunostimulatory oligonucleotide comprises a CpG motif having the formula 5'X<sub>1</sub>CGX<sub>2</sub>3', wherein X<sub>1</sub> is adenine, guanine, or thymine, and X<sub>2</sub> is cytosine, thymine, or adenine.

28. (currently amended) The immune adjuvant composition as claimed in claim 19 or 23, wherein the immunostimulatory oligonucleotide comprises TCTCCCAGCGTGCGCCAT (SEQ ID NO:1).

29-62. (canceled)

63. (currently amended) An immune adjuvant composition comprising  
(a) a saponin possessing immune adjuvant activity, wherein the saponin is derived from *Quillaja saponaria*; and

(b) an immunostimulatory oligonucleotide comprising at least one unmethylated CpG dinucleotide,

wherein the saponin ~~comprises~~ is substantially pure, and the saponin is QS-7, QS-17 or QS-18, and

wherein the saponin and immunostimulatory oligonucleotide have a synergistic adjuvant effect.

64. (previously presented) A method for inducing an immune response in an individual to an antigen comprising (1) administering an amount of the immune adjuvant composition as claimed in claim 63 to the individual; and (2) administering a nucleic acid molecule comprising a nucleotide sequence encoding the antigen to the individual, wherein (1) and (2) induce an immune response in the individual to the antigen.

65. (currently amended) An immune adjuvant composition comprising  
(a) a saponin possessing immune adjuvant activity, wherein the saponin is derived from *Quillaja saponaria*; and

(b) an immunostimulatory oligonucleotide comprising at least one unmethylated CpG dinucleotide,

wherein the immunostimulatory oligonucleotide comprises at least one chemical group selected from the group consisting of phosphorothioate, alkylphosphonate,

phosphorodithioate, alkylphosphorothioate, phosphoramidate, 2-O-methyl, carbamate, acetamidate, carboxymethyl ester, carbonate, and phosphate triester, and

wherein the saponin and immunostimulatory oligonucleotide have a synergistic adjuvant effect.

66. (previously presented) The immune adjuvant composition as claimed in claim 65, wherein the immunostimulatory oligonucleotide comprises at least one phosphorothioate modified nucleotide.

67. (previously presented) A method for inducing an immune response in an individual to an antigen comprising (1) administering an amount of the immune adjuvant composition as claimed in claim 65 to the individual; and (2) administering a nucleic acid molecule comprising a nucleotide sequence encoding the antigen to the individual, wherein (1) and (2) induce an immune response in the individual to the antigen.

68. (previously presented) A method for inducing an immune response in an individual to an antigen comprising (1) administering an amount of the immune adjuvant composition as claimed in claim 66 to the individual; and (2) administering a nucleic acid molecule comprising a nucleotide sequence encoding the antigen to the individual, wherein (1) and (2) induce an immune response in the individual to the antigen.

69. (currently amended) An immune adjuvant composition comprising  
(a) a saponin possessing immune adjuvant activity, wherein the saponin is derived from *Quillaja saponaria*; and  
(b) an immunostimulatory oligonucleotide comprising at least one unmethylated CpG dinucleotide,

wherein the immunostimulatory oligonucleotide comprises  
TCTCCCAGCGTGCGCCAT (SEQ ID NO:1), and

wherein the saponin and immunostimulatory oligonucleotide have a synergistic adjuvant effect.

70. (previously presented) A method for inducing an immune response in an individual to an antigen comprising (1) administering an amount of the immune adjuvant composition as claimed in claim 69 to the individual; and (2) administering a nucleic acid molecule comprising a nucleotide sequence encoding the antigen to the individual, wherein (1) and (2) induce an immune response in the individual to the antigen.

71. (currently amended) An immune adjuvant composition comprising

(a) a saponin possessing immune adjuvant activity, wherein the saponin is derived from *Quillaja saponaria*; and

(b) an immunostimulatory oligonucleotide comprising at least one unmethylated CpG dinucleotide,

wherein the immunostimulatory oligonucleotide comprises TCCATGACGTTCTGACGTT (SEQ ID NO:2), and

wherein the saponin and immunostimulatory oligonucleotide have a synergistic adjuvant effect.

72. (previously presented) A method for inducing an immune response in an individual to an antigen comprising (1) administering an amount of the immune adjuvant composition as claimed in claim 71 to the individual; and (2) administering a nucleic acid molecule comprising a nucleotide sequence encoding the antigen to the individual, wherein (1) and (2) induce an immune response in the individual to the antigen.

73. (currently amended) An immune adjuvant composition comprising

(a) a saponin possessing immune adjuvant activity, wherein the saponin is derived from *Quillaja saponaria*; and

(b) an immunostimulatory oligonucleotide comprising at least one unmethylated CpG dinucleotide, wherein the immunostimulatory oligonucleotide is 4-40 bases in length, and

wherein the saponin and immunostimulatory oligonucleotide have a synergistic adjuvant effect.

74. (previously presented) A method for inducing an immune response in an individual to an antigen comprising (1) administering an amount of the immune adjuvant composition as claimed in claim 73 to the individual; and (2) administering a nucleic acid molecule comprising a nucleotide sequence encoding the antigen to the individual, wherein (1) and (2) induce an immune response in the individual to the antigen.

75. (currently amended) An immune adjuvant composition comprising

(a) a saponin possessing immune adjuvant activity, wherein the saponin (i) is derived from *Quillaja saponaria* and (ii) is a chemically modified saponin; and

(b) an immunostimulatory oligonucleotide comprising at least one unmethylated CpG dinucleotide,



wherein the saponin and immunostimulatory oligonucleotide have a synergistic adjuvant effect.

76. (previously presented) A method for inducing an immune response in an individual to an antigen comprising (1) administering an amount of the immune adjuvant composition as claimed in claim 75 to the individual; and (2) administering a nucleic acid molecule comprising a nucleotide sequence encoding the antigen to the individual, wherein (1) and (2) induce an immune response in the individual to the antigen.

77. (previously presented) The composition of claim 19, wherein the saponin is a chemically modified saponin.

78. (currently amended) The immune adjuvant composition as claimed in claim 19 or 23, wherein the immunostimulatory oligonucleotide comprises TCCATGACGTTCTGACGTT (SEQ ID NO:2).

79-89. (canceled)

90. (previously presented) A method for inducing an immune response in an individual to an antigen comprising (1) administering an amount of the immune adjuvant composition as claimed in claim 19 to the individual; and (2) administering a nucleic acid molecule comprising a nucleotide sequence encoding the antigen to the individual, wherein (1) and (2) induce an immune response in the individual to the antigen.

91. (canceled)

92. (currently amended) The method as claimed in any of claims 64, 67, 68, 70, 72, 74, 76, or 90, wherein the saponin ~~comprises~~ is a substantially pure saponin.

93. (currently amended) The method as claimed in claim 92, wherein the substantially pure saponin ~~comprises~~ is QS-7, QS-17, QS-18, or QS-21.

94. (currently amended) The method as claimed in claim 93, wherein the substantially pure saponin ~~comprises~~ is QS-21.

95. (previously presented) The method as claimed in any of claims 64, 67, 68, 70, 72, 74, 76, or 90, wherein the immunostimulatory oligonucleotide comprises more than one unmethylated CpG dinucleotide.

96. (previously presented) The method as claimed in any of claims 64, 70, 72, 74, 76, or 90, wherein the immunostimulatory oligonucleotide comprises at least one chemical

group selected from the group consisting of phosphorothioate, alkylphosphonate, phosphorodithioate, alkylphosphorothioate, phosphoramidate, 2-O-methyl, carbamate, acetamidate, carboxymethyl ester, carbonate, and phosphate triester.

97. (previously presented) The method as claimed in any of claims 64, 70, 72, 74, 76, or 90, wherein the immunostimulatory oligonucleotide comprises at least one phosphorothioate modified nucleotide.

98. (previously presented) The method as claimed in any of claims 64, 67, 68, 70, 72, 74, 76, or 90, wherein the immunostimulatory oligonucleotide comprises a CpG motif having the formula 5' $X_1$ CG $X_2$ 3', wherein  $X_1$  is adenine, guanine, or thymine, and  $X_2$  is cytosine, thymine, or adenine.

99. (previously presented) The method as claimed in any of claims 64, 67, 68, 74, 76, or 90, wherein the immunostimulatory oligonucleotide comprises TCTCCCAGCGTGCGCCAT (SEQ ID NO:1) or TCCATGACGTTCTGACGTT (SEQ ID NO:2).

100. (previously presented) The method as claimed in any of claims 64, 67, 68, 70, 72, 74, 76, or 90, wherein the individual is an animal.

101. (previously presented) The method as claimed in claim 100, wherein the animal is a mammal.

102. (previously presented) The method as claimed in any of claims 64, 67, 68, 70, 72, 74, 76, or 90, wherein the individual is a human.

103. (currently amended) ~~An~~ A vaccine composition comprising

(a) a saponin possessing immune adjuvant activity, wherein the saponin is derived from *Quillaja saponaria*;

(b) an immunostimulatory oligonucleotide comprising at least one unmethylated CpG dinucleotide; and

(c) a nucleic acid molecule comprising a nucleotide sequence encoding an antigen, wherein the nucleotide sequence is operatively linked to a promoter,

wherein the immunostimulatory oligonucleotide is not a part of the nucleic acid molecule comprising the nucleotide sequence encoding the antigen.

104. (canceled)

105. (currently amended) The vaccine composition as claimed in claim 103, wherein the saponin ~~comprises~~ is a substantially pure saponin.

106. (currently amended) The vaccine composition as claimed in claim 105, wherein the substantially pure saponin ~~comprises~~ is QS-7, QS-17, QS-18, or QS-21.

107. (currently amended) The vaccine composition as claimed in claim 106, wherein the substantially pure saponin ~~comprises~~ is QS-21.

108. (previously presented) The vaccine composition as claimed in claim 103, wherein the immunostimulatory oligonucleotide comprises more than one unmethylated CpG dinucleotide.

109. (currently amended) The vaccine composition as claimed in claim 103, wherein the immunostimulatory oligonucleotide comprises ~~one or more chemical groups at least one chemical group~~ selected from the group consisting of phosphorothioate, alkylphosphonate, phosphorodithioate, alkylphosphorothioate, phosphoramidate, 2-O-methyl, carbamate, acetamidate, carboxymethyl ester, carbonate, and phosphate triester.

110. (previously presented) The vaccine composition as claimed in claim 103, wherein the immunostimulatory oligonucleotide comprises at least one phosphorothioate modified nucleotide.

111. (previously presented) The vaccine composition as claimed in claim 103, wherein the immunostimulatory oligonucleotide comprises a CpG motif having the formula 5'X<sub>1</sub>CGX<sub>2</sub>3', wherein X<sub>1</sub> is adenine, guanine, or thymine, and X<sub>2</sub> is cytosine, thymine, or adenine.

112. (currently amended) The vaccine composition as claimed in claim 103 or 107, wherein the immunostimulatory oligonucleotide comprises TCTCCCAGCGTGCGCCAT (SEQ ID NO:1) or TCCATGACGTTCTGACGTT (SEQ ID NO:2).

113. (canceled)

114. (currently amended) The method of ~~claim 113~~ any of claims 64, 70, 72, 76, or 90, wherein the nucleic acid molecule encoding the antigen is administered to the individual concurrently with the immune adjuvant composition.

115-126. (canceled)

127. (canceled)

128. (currently amended) The method of ~~claim 127~~ any of claims 67, 68, or 74, wherein the nucleic acid molecule encoding the antigen is administered to the individual concurrently with the immune adjuvant composition.

129-149. (canceled)

150. (new) The method as claimed in any of claims 67, 68, 74, 76, and 90, wherein the saponin is substantially pure, wherein the saponin is QS-21, and wherein the immunostimulatory oligonucleotide comprises TCTCCCAGCGTGCGCCAT (SEQ ID NO:1) or TCCATGACGTTCCTGACGTT (SEQ ID NO:2).

151. (new) The immune adjuvant composition as claimed in claim 65 or 73, wherein the saponin is chemically modified.

152. (new) The immune adjuvant composition as claimed in claim 65, 73 or 75, wherein the immunostimulatory oligonucleotide comprises TCTCCCAGCGTGCGCCAT (SEQ ID NO:1) or TCCATGACGTTCCTGACGTT (SEQ ID NO:2).

153. (new) The immune adjuvant composition as claimed in claim 65 or 75, wherein the saponin is substantially pure.

154. (new) The immune adjuvant composition as claimed in claim 153, wherein the saponin is QS-21.

155. (new) The immune adjuvant composition as claimed in claim 154, wherein the immunostimulatory oligonucleotide comprises TCTCCCAGCGTGCGCCAT (SEQ ID NO:1) or TCCATGACGTTCCTGACGTT (SEQ ID NO:2).

156. (new) The immune adjuvant composition as claimed in claim 73, wherein the saponin is substantially pure.

157. (new) The immune adjuvant composition as claimed in claim 156, wherein the saponin is QS-21.

158. (new) The immune adjuvant composition as claimed in claim 73 or 157, wherein the immunostimulatory oligonucleotide comprises at least one chemical group selected from the group consisting of phosphorothioate, alkylphosphonate, phosphorodithioate, alkylphosphorothioate, phosphoramidate, 2-O-methyl, carbamate, acetamidate, carboxymethyl ester, carbonate, and phosphate triester.



159. (new) The immune adjuvant composition as claimed in claim 157, wherein the immunostimulatory oligonucleotide comprises TCTCCCAGCGTGCGCCAT (SEQ ID NO:1) or TCCATGACG TTCCTGACGTT (SEQ ID NO:2).

160. (new) The immune adjuvant composition as claimed in claim 69 or 71, wherein the saponin is substantially pure.

161. (new) The immune adjuvant composition as claimed in claim 160, wherein the saponin is QS-21.